REMARKS

After entry of this amendment, claims 1-9 and 11-29 are pending. Claim 10 is cancelled; claims 1, 5-9, 11, 15-17, 20-22 and 29 are amended.

I. 35 U.S.C. § 112 Rejections

Reconsideration is respectfully requested of the rejection of claims 1-9 and 11-29 under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. As explained in the prior response, applicant respectfully maintains that the pending claims are fully enabled. However, to expedite prosecution, the claims have been amended so they are directed to the treatment of alopecia arising from radiation exposure. Because the Office stated that the specification was "enabling for the treatment of alopecia,"[1] these amendments obviate the current rejections.

Further, the Office states that treatment is not enabled with respect to the genus of methionine-like moieties defined in claim 1 because the specification and Declarations do not "provide any reasonable or sound scientific reasoning as to why the activity observed with D-methionine would also have been representative of each member of the genus of compounds encompassed by the formula defined in present claim 1."[2] However, Applicant respectfully submits that the specification is enabling of the invention as claimed and the Office has not pointed to any evidence that is inconsistent with the applicant's assertions in the specification. Applicant states in the specification that

> [a]nalogs or derivatives of methionine useful in the present invention are compounds containing a methionine moiety, or a methionine-like moiety including a thioether group, that exhibit an ... alopecia protectant effect ... when used in conjunction with ... exposure to ... radiation.[3]

Beyond the common thioether group, the generically defined compound shares the basic molecular structure of methionine, and indeed is further characterized in

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[1] Page 4 of the Office action dated March 8, 2006.
[2] Page 13 of the Office action dated March 8, 2006.
[3] Page 27 of the specification.

the claim itself as "containing a methionine or methionine-like moiety." Thus, the specification and claims define a relatively narrow class of compounds having a structure that one skilled in the art would reasonably expect to be effective in the same manner as D-methionine. In view of the teaching provided by Applicant's disclosure, confirmation of enablement as to any particular species within this genus would require no more than routine experimentation.

Denial of generic protection would invite those skilled in the art to appropriate with impunity the advance in the art provided by Applicant's disclosure. In order to reasonably and adequately protect Applicant's invention, it is respectfully submitted that generic claim 1 should be allowed and issued.

The Examiner has cited the data presented in the working examples as not fully representing the genus and therefore failing to establish enablement. But, the court in *In re Marzocchi* held that:

> "it is incumbent on the Patent Office whenever a rejection [for enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in the supporting disclosure and to back up such assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."[4]

It is applicant's understanding that the Examiner is citing the breadth of the claim alone as meeting the burden imposed by *Marzocchi*. However, rejection for breadth alone is not appropriate, as explained in *In Re Borkowski*,[5] *In re Robins*,[6] and in *Marzocchi* itself. In this case, the experimentation required to test for each agent's protectant efficacy to protect against alopecia is not undue because a person of ordinary skill would know how to test each agent for its ability to treat alopecia and such testing would be routine. Thus, the claims as amended satisfy the enablement requirement of 35 U.S.C. § 112.

Moreover, claims 12, 13, and 22 limit the protective agent to D-methionine, L-methionine, or DL-methionine. Therefore, the experimentation required to test

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[4] In re Marzocchi, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).
[5] 164 U.S.P.Q. 642 (C.C.P.A. 1970).
[6] 166 U.S.P.Q. 552 (C.C.P.A. 1970).

for each agent's protectant efficacy against alopecia is certainly not undue. Thus, claims 12, 13, and 22 satisfy the enablement requirement of 35 U.S.C. § 112.

Further, the amended claims recite methods of “treating alopecia in a patient exposed to radiation.” The definition of “treat” is to care for a patient medically or surgically.[7] When read in the context of the claims and specification as a whole, the meaning of treating alopecia is to administer the protective agent of the invention to a subject in need thereof; this administration could be prior to, simultaneous with or subsequent to the onset of alopecia. Thus, claim 1 encompasses prophylactic administration prior to the onset of alopecia which may not absolutely "prevent" alopecia in the patient, but serves to inhibit or control this condition.

Applicant respectfully disagrees with the Examiner's construction of "preventing" as meaning "absolutely preventing.[8] However, by amendment of the claims to delete the term "preventing" this issue is obviated from the examination of the instant application without sacrifice of scope with respect to prophylactic administration, administration simultaneous with onset, and/or administration subsequent to onset. Applicant's respectfully reserve the right to further contest the meaning of "preventing" in successor applications directed to administration of a compound containing a methionine or methionine-like moiety to patients at risk for other conditions caused by radiation, i.e., mucositis, ototoxicity, neurotoxicity, gastrointestinal conditions, etc.

Reconsideration is respectfully requested of the rejection of claims 5-9, 15-17, 20-22 and 29 as being indefinite. To expedite prosecution, these claims have been amended to remove the term "about," and thus, this rejection is moot.

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[7] Stedman's Medical Dictionary, 26th Ed., 1995.

[8] In fact, it appears that the Examiner's own comments would lead to a construction of "preventing" as not necessarily absolute. Cf. p. 7 of the March 8, 2006 Office action.

The Claimed Compounds are Not *prima facie* Obvious in View of the Claims of the Cited Patents.

Reconsideration is requested of the rejection of claims 1-9 and 11-29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,187,817, U.S. Patent No. 6,265,386, U.S. Patent Application No. 09/911,195 and of the provisional rejection of claims 1-9 and 11-29 over the claims of U.S. Patent Application Nos. 10/694,436, 10/694,448, and 11/324,744.

The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.[9] However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.[10]

It is respectfully submitted that the subject matter of the claims of the present application would not have been obvious in view of the claims of U.S. Patent Nos. 6,187,817 and 6,265,386 or U.S. Patent Application Nos. 09/911,195, 10/694,436, 10/694,448, and 11/324,744. When evaluating the scope of a claim, every element of the claim must be considered.[11] To support an obviousness-type double patenting rejection, the claims must have been obvious at the time of filing and not merely obvious upon hindsight reconstruction using applicant's disclosure as a template to arrive at the features of the instantly claimed methods from the claims of the '817 and '386 patents and the ‘195, ‘436, '448, and ‘744 applications. It is respectfully submitted that the Office has failed to establish obviousness based on any reference or by evidence of the level of

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[9] In re Braat, 937 F.2d 589 (Fed. Cir. 1991).
[10] Purdue Pharma L.P. v. Boehringer Ingelheim GMbH, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).
[11] See, e.g., In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995).

skill in the art or the nature of the problem that is not based upon impermissible hindsight reconstruction.

A. U.S. Patent No. 6,187,817

Subject claims 1-9 and 11-29 are directed to methods for treating alopecia in a patient exposed to radiation, the method comprising administering to said patient an effective amount of a protective agent. In contrast, claims 1-28 of the '817 patent are directed to a method for preventing or reducing ototoxicity, claims 29-30 are directed to methods of preventing or reducing weight loss, claims 31-32 are directed to methods of preventing or reducing gastrointestinal toxicity, claims 33-34 are directed to methods of preventing or reducing neurotoxicity, and claims 35-36 are directed to methods of preventing or reducing alopecia wherein all of these conditions arise from treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound. Accordingly, because the claims of the '817 patent are not directed to protection of toxicities arising from radiation exposure, the claims do not include all the elements of the subject claims.

Further, the mechanisms of cell damage are different for different insults (e.g., platinum-coordination compounds versus radiation) and a person of ordinary skill would not have known that a protective agent for toxicities arising from platinum-coordination compounds would necessarily be effective as a protective agent against toxicities arising from radiation. Moreover, without applicant's own disclosure regarding the protection against alopecia arising from radiation, a person of ordinary skill would not have found the instant claims obvious upon examination of the cited art. Thus, the subject claims would not have been obvious from the claims of the '817 patent.

B. U.S. Patent No. 6,265,386

The subject claims are detailed above for the '817 patent. Claims 1-25 of the '386 patent are directed to a method for preventing or treating ototoxicity in a patient undergoing treatment with an aminoglycoside antibiotic comprising administering to said patient an effective amount of an otoprotective agent.

Accordingly, as the claims of the ‘386 patent do not include the element of a “treating alopecia,” the claims do not include all the elements of the subject claims. Further, a person of ordinary skill would not have found the instant claims for “treating alopecia” obvious from the '386 claims because the claims of the ‘386 patent are directed to "treating or preventing ototoxicity." Further, there are differences in the mechanisms of cell damage arising from aminoglycoside antibiotics and from radiation. Thus, only impermissible hindsight would have allowed such a person of ordinary skill to have found the instant claims obvious.

C. U.S. Application Serial No. 09/911,195

The claims of the ‘195 application are directed to methods for preventing or treating ototoxicity in a patient exposed to noise. Further, there are differences in the mechanisms of cell damage arising from noise and from radiation. Thus, only impermissible hindsight would have allowed a person of ordinary skill to have found the instant claims obvious from the claims of the '195 application.

D. U.S. Application Serial No. 10/694,436

The claims of the ‘436 application are directed to methods for preventing or treating mucositis in a patient undergoing treatment with an anti-tumor platinum-coordination compound or exposed to radiation. Further, the mechanisms of cell damage resulting in mucositis are different than the mechanisms of cell damage resulting in alopecia. Thus, only impermissible hindsight using applicant's specification as a template would have allowed a person of ordinary skill to have found the instant claims obvious from the claims of the '436 application.

E. U.S. Application Serial No. 10/694,448

The claims of the ‘448 application are directed to methods for preventing or treating ototoxicity in a patient undergoing treatment with an aminoglycoside antibiotic or a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound comprising administering to said patient an effective amount of an otoprotective agent. Further, there are differences in the mechanisms of cell damage arising from anti-tumor platinum-coordination

compounds, aminoglycoside antibiotics, and from radiation. Thus, only impermissible hindsight would have allowed a person of ordinary skill to have found the instant claims obvious.

F. U.S. Application Serial No. 11/324,744

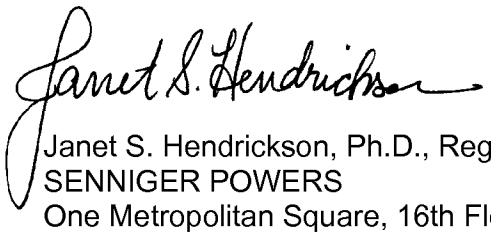
The claims of the '744 application are directed to methods for preventing or treating ototoxicity in a patient exposed to noise. Further, there are differences in the mechanisms of cell damage arising from noise and from radiation. Thus, only impermissible hindsight would have allowed a person of ordinary skill to have found the instant claims obvious from the claims of the '744 application.

In summary, a person of ordinary skill would not have found the instant methods for the treatment of alopecia arising from exposure to radiation obvious upon consideration of the claims of the cited patents and applications. It is, therefore, respectfully requested that the double patenting rejection over the claims of the '817 and '386 patents and the '195, '436, '448, and '744 applications be withdrawn.

Applicant submits that the present application is now in a condition for allowance and requests early allowance of the pending claims.

A check in the amount of $60.00 for a one month extension of time is enclosed. The Commissioner is hereby authorized to charge any underpayment and credit any overpayment of government fees to Deposit Account No. 19-1345.

Respectfully submitted,



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